

In the Sequence Listing:

Please insert a paper copy (pages 1-2) of the Sequence Listing after the abstract in the above-captioned patent application. A computer readable form (CRF copy) of the Sequence Listing accompanies this response.

AMENDMENTS

In the Specification:

Please replace paragraph [0007] beginning on page 2 with the following rewritten paragraph:

[0007] In an embodiment, the nucleotide sequence is from human immunodeficiency virus (HIV, *e.g.*, HIV-1 or HIV-2) and comprises the sequences TTG₆TA (SEQ ID NO:1), CAG₄AA (SEQ ID NO:2), or both. In the latter nucleotide sequences, one or more nucleotides flanking the G₆ and G₄ stretches sometimes are substituted by another nucleotide (*e.g.*, one or more of the TT or TA flanking the G₆ stretch or CA or AA flanking the G₄ stretch sometimes are substituted by another nucleotide). In related embodiments, the nucleic acid includes additional sequences flanking the G₆ or G₄ stretches from an HIV strain, and in specific embodiments, the nucleic acid comprises or consists of the nucleotide sequence TTGGGGGGTACAGTGCAGGGGAA (SEQ ID NO:3).

Please replace paragraph [0017] beginning on page 6 and bridging to page 7 with the following rewritten paragraph:

[0017] Often, a nucleic acid capable of forming one or more secondary structures includes a nucleotide sequence identical to a native nucleotide sequence present in the central flap of a retrovirus. The central flap is a single-stranded region in mostly double-stranded transcription product of a retrovirus. Retroviruses include but are not limited to human immunodeficiency virus (HIV), the causative agent of human auto-immunodeficiency syndrome (AIDS), and the simian immunodeficiency virus (SIV). The non-primate lentiviral group includes the prototype "slow virus" visna/maedi virus (VMV), as well as the related caprine arthritis-encephalitis virus (CAEV), equine infectious anaemia virus (EIAV) and the more recently described feline immunodeficiency virus (FIV), bovine immunodeficiency virus (BIV), murine leukemia virus (MLV), human immunodeficiency virus (HIV), equine infectious anaemia virus (EIAV), mouse mammary tumour virus (MMTV), Rous sarcoma virus (RSV), Fujinami sarcoma virus (FuSV), Moloney murine leukemia virus (Mo-MLV), FBR murine osteosarcoma virus (FBR MSV), Moloney murine sarcoma virus (Mo-MSV), Abelson murine leukemia virus (A-MLV), Avian myelocytomatosis virus-29 (MC29), and Avian erythroblastosis virus (AEV). In an embodiment, the nucleotide sequence is from

human immunodeficiency virus (HIV, e.g., HIV-1 or HIV-2) and comprises the sequences TTG₆TA (SEQ ID NO:1) (sometimes referred to as the G₆ stretch), CAG₄AA (SEQ ID NO:2) (sometimes referred to as the G₄ stretch), or both. In the latter nucleotide sequences, one or more nucleotides flanking the G₆ and G₄ stretches sometimes are substituted by another nucleotide (e.g., one or more of the TT or TA flanking the G₆ stretch or CA or AA flanking the G₄ stretch sometimes are substituted by another nucleotide). In related embodiments, the nucleic acid includes additional sequences flanking the G₆ or G₄ stretches from an HIV strain published in a publically available database (see e.g., [http address hiv-web.lanl.gov](http://hiv-web.lanl.gov)), and in specific embodiments, the nucleic acid comprises or consists of the nucleotide sequence TTGGGGGGTACAGTGCAGGGGAA (SEQ ID NO:3). The nucleic acid usually does not consist of the nucleic acid sequences TTG₆TACAGTGCA (SEQ ID NO:4); TTG₆TACAGTGCAG₄AAA (SEQ ID NO:5) or TTG₆TACAGTGCAG₄AAAGAATAGTAGACATAATAGCAACAGAC (SEQ ID NO:6).

Please replace paragraph [0045] beginning on page 17 with the following rewritten paragraph:

[0045] A polymerase arrest assay is useful for determining whether transcription is modulated by a candidate molecule and/or a nucleic acid binding protein. Such an assay includes a template nucleic acid, which often comprises a quadruplex forming sequence, and a primer nucleic acid which hybridizes to the template nucleic acid 5' of the quadruplex-forming sequence. The primer is extended by a polymerase (e.g., Taq polymerase), which advances from the primer along the template nucleic acid. In this assay, a quadruplex structure can block or arrest the advance of the enzyme, leading to shorter transcription fragments. Also, the arrest assay may be conducted at a variety of temperatures, including 45°C and 60°C, and at a variety of ion concentrations. An example of the Taq polymerase stop assay is described in Han, *et al.*, *Nucl. Acids Res.* 27:537-542 (1999), which is a modification of that used by Weitzmann, *et al.*, *J. Biol. Chem.* 271, 20958–20964 (1996). Briefly, a reaction mixture of template DNA (50 nM), Tris•HCl (50 mM), MgCl₂ (10 mM), DTT (0.5 mM), EDTA (0.1 mM), BSA (60 ng), and 5'-end-labeled quadruplex nucleic acid (~18 nM) is heated to 90°C for 5 minutes and allowed to cool to ambient temperature over 30 minutes. Taq Polymerase (1 µl) is added to the reaction mixture, and the reaction is maintained at a constant temperature for 30 minutes. Following the addition of 10 µl stop buffer (formamide (20 ml), 1 M NaOH (200 µl), 0.5 M EDTA (400 µl), and 10 mg

bromophenol blue), the reactions are separated on a preparative gel (12%) and visualized on a phosphorimager. Adenine sequencing (indicated by "A" at the top of the gel) is performed using double-stranded DNA Cycle Sequencing System from Life Technologies. The general sequence for the template strands is TCCAACATGTATAC (SEQ ID NO:7)-INSERT-TTAGCGACACGCAATTGCTATAGTGAGTCGTATTA (SEQ ID NO:8). Bands on the gel that exhibit slower mobility are indicative of quadruplex formation.

Please replace paragraph [0046] beginning on page 17 and bridging to page 18 with the following rewritten paragraph:

[0046] Another example of a polymerase arrest assay can be used in a medium to high throughput format. In this assay embodiment, a 5'- fluorescent-labeled (FAM) primer (P45, 15 nM) is mixed with template DNA (15nM) in a Tris-HCL buffer (15 mM Tris, pH 7.5) containing 10mM MgCl₂, 0.1mM EDTA and 0.1mM mixed deoxynucleotide triphosphates (dNTP's). The assay is performed by copying a template with a polymerase, where the copy is primed from a fluorescently labeled primer nucleic acid (*e.g.*, a suitable fluorescent label is FAM). The template comprises a sequence from the central flap region capable of forming a quadruplex and the primer is a smaller nucleic acid complementary to a region upstream of the sequence in the template capable of forming the quadruplex. In an example of a template and primer for detecting quadruplex formation in the *CMYC* promoter, the FAM-P45 primer (5'- 6FAM-AGTCTGACTGACTGTACGTAGCTAATACGACTCACTATAGCAATT-3') (SEQ ID NO:9) and the template DNA (5'-TCCAACATGTATACTGGGGA GGGTGGGGAGGGTGGGGAAGGTT AGCGACACGCAATTGCTATAG TGAGTCGTATTAGCTACGTACAGTCAGTCAGACT-3') (SEQ ID NO:10) are synthesized and HPLC purified by Applied Biosystems. The mixture is denatured at 95°C for 5 minutes and, after cooling down to room temperature, is incubated at 37°C for 15 minutes. After cooling down to room temperature, 1mM KCl₂ and the test compound (various concentrations) are added and the mixture incubated for 15 minutes at room temperature. The primer extension is performed by adding 10mM KCl and Taq DNA Polymerase (2.5 U/reaction, Promega) and incubating at 70°C for 30 minutes. The reaction is stopped by adding 1 µl of the reaction mixture to 10 µl Hi-Di Formamide mixed and 0.25 µl LIZ120 size standard. Hi-Di Formamide and LIZ120 size standard are purchased from Applied Biosystems. The partially extended quadruplex arrest product is between 61 or 62 bases long and the full-length extended product is 99 bases long. The products are separated and

analyzed using capillary electrophoresis. Capillary electrophoresis is performed using an ABI PRISM 3100-Avant Genetic Analyzer.